UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,280	11/07/2001	Yongming Sun	DEX-0257	3559

26259 7590 08/13/2004

LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,280	SUN ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8,15 and 18-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8,15 and 18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed June 23, 2004. Claims 1-17 were previously pending, with claims 6, 9-14 and 16 withdrawn from consideration. Applicants cancelled claims 6, 9-14, 16 and 17, amended claims 1 and 15, and added new claims 18-27. Claims 1-5, 7, 8, 15 and 18-27 are pending and will be examined to the degree that they read on originally elected SEQ ID NO: 112-115.

2. Applicants' claim cancellations and arguments overcame the following rejections: rejection of claim 17 under 35 U.S.C. 101, utility; rejection of claim 17 under 35 U.S.C. first paragraph, enablement; rejection of claim 14 under 35 U.S.C. 112, second paragraph. All other rejections are maintained for reasons given in the "Response to Arguments" section below.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on June 23, 2004 was filed after the mailing date of the first office action on January 22, 2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

4. Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1-5, 7, 8 and 15 under 35 U.S.C. 101, utility, and the rejection under 35 U.S.C. 112, first paragraph, enablement, Applicants argue that from the description of SEQ ID NO: 112-115 it is clear that SEQ ID NO: 112-115 show differential expression in cancer tissue, and that "The case law on utility is quite clear; mere identification of a pharmacological activity of a claimed compound that is relevant to an asserted pharmacological use

provides an immediate benefit to the public and thus satisfies the utility requirement. Nelson' v. Bowler, 626 F-2d 853, 206 USPQ 881, 883 (CCPA 1980)."

However, Applicants did not show either that the nucleic acids with SEQ ID NO: 112-115 are expressed only in cancer tissue or that they have any "pharmacological activity". The only fact Applicants can assert with respect to SEQ ID NO: 112-115 is that these sequences seem to be expressed in ovarian tissue based on the results of a computerized database search of a single database. Such data is totally inconclusive, as other databases or results published somewhere else may show that SEQ ID NO: 112-115 are expressed in normal ovarian tissue as well. Further, even if one were to rely on that single database, the question of the comparative level of expression of SEQ ID NO: 112-115 in cancerous vs. normal tissue, critical to the utility of SEQ ID NO: 112-115 as being indicative of tumorogenesis, remains unanswered. In order for SEQ ID NO: 112-115 to be diagnostic for prostate cancer, their level of expression in prostate cancer cells would have to be significantly higher than in normal prostate cells. Applicants have not provided a conclusive evidence that this is indeed the case.

The rejections are maintained.

B) Regarding the rejection of claims 1-5, 7 and 8 under 35 U.S.C. 112, first paragraph, written description, Applicants argue that the amendment to claim 1, introducing a limitation of stringent hybridization conditions to part c) and a limitation of at least 80% sequence identity in part (d), as well as the limitation of being differentially expressed in ovarian cancer tissue, overcomes the rejection.

However, Applicants did not describe any nucleic acids which hybridize to SEQ ID NO: 112-115 under stringent conditions, or any nucleic acids which have at least 80% sequence identity to SEQ ID NO: 112-115. Further, the limitation of the nucleic acid being differentially expressed in

ovarian cancer tissue is not relevant, as it does not impose any structural limitation on the nucleic acid sequence, and there are thousands of nucleic acids which are differentially expressed in ovarian cancer tissue.

The rejection is maintained.

C) Regarding the rejection of claims 1, 2, 4, 5, 7 and 8 under 35 U. S. C. 102(a) as anticipated by a sequence with accession No. BF116062, Applicants argue that this sequence would not hybridize to SEQ ID NO: 115 under stringent hybridization conditions because of regions of sequence disparity. However, the sequence with accession No. BF116062 is 99.8% identical (one mismatch) over 582 bp to SEQ ID NO: 115, therefore it would hybridize to SEQ ID NO: 115 under stringent hybridization conditions.

The rejection is maintained.

D) Regarding the rejection of claims 1, 2, 4, 5, 7 and 8 under 35 U. S. C. 102(a) as anticipated by a sequence with accession No. BE857462, Applicants argue that this sequence would not hybridize to SEQ ID NO: 112 or 113 under stringent hybridization conditions because of regions of sequence disparity. However, the sequence with accession No. BE857462 is 99.4% identical (one mismatch) over 165 bp to SEQ ID NO: 112, therefore it would hybridize to SEQ ID NO: 112 under stringent hybridization conditions. Further, the sequence with accession No. BE857462 is 99.8% identical (one mismatch) over 524 bp to SEQ ID NO: 113, therefore it would hybridize to SEQ ID NO: 113 under stringent hybridization conditions.

The rejection is maintained.

E) Regarding the rejection of claims 1, 2, 4, 5, 7 and 8 under 35 U. S. C. 102(b) as anticipated by a sequence with accession No. AA156960, Applicants argue that this sequence would not hybridize to SEQ ID NO: 115 or 114 under stringent hybridization conditions because of

regions of sequence disparity. However, the sequence with accession No. No. AA156960 is 99.6% identical (two mismatches) over 495 bp to SEQ ID NO: 115, therefore it would hybridize to SEQ ID NO: 115 under stringent hybridization conditions. Further, the sequence with accession No. No. AA156960 is 99.6% identical (two mismatches) over 495 bp to SEQ ID NO: 114, therefore it would hybridize to SEQ ID NO: 114 under stringent hybridization conditions.

The rejection is maintained.

F) Regarding the rejection of claims 1, 2, 4, 5, 7 and 8 under 35 U. S. C. 102(b) as anticipated by a sequence with accession No. AA088637, Applicants argue that this sequence would not hybridize to SEQ ID NO: 113 or 112 under stringent hybridization conditions because of regions of sequence disparity. However, the sequence with accession No. AA088637 is 91.6% over 405 bp to SEQ ID NO: 113, with 171 contiguous nucleotides (bp 141-311) 100% identical to SEQ ID NO: 113, therefore it would hybridize to SEQ ID NO: 113 under stringent hybridization conditions. Further, the sequence with accession No. AA088637 is 87.8% identical over 165 bp to SEQ ID NO: 112, with 56 contiguous nucleotides (bp 1-56) 100% identical to SEQ ID NO: 112, therefore it would hybridize to SEQ ID NO: 112 under stringent hybridization conditions.

The rejection is maintained.

G) Regarding the rejection of claims 1, 2, 4, 5, 8, 15 and 17 under 35 U.S.C. 102(e) as anticipated by Rosen et al., Applicants argue that this sequence with SEQ ID NO: 947 taught by Rosen et al. would not hybridize to SEQ ID NO: 112-115 under stringent hybridization conditions because of regions of sequence disparity. However, the sequence with SEQ ID NO: 947 is 100% identical over 613 nucleotides (bp 1393-2005) and 586 nucleotides (bp 2153-2738) to SEQ ID NO: 115, therefore it would hybridize to SEQ ID NO: 115 under stringent hybridization conditions. The sequence with SEQ ID NO: 947 is 100% identical over 576 nucleotides (bp 343-918) to SEQ ID

NO: 114, therefore it would hybridize to SEQ ID NO: 114 under stringent hybridization conditions. The sequence with SEQ ID NO: 947 is also 100% identical over 407 nucleotides (bp 242-648) to SEQ ID NO: 113, therefore it would hybridize to SEQ ID NO: 113 under stringent hybridization conditions. Finally, the sequence with SEQ ID NO: 947 is 100% identical over 291 nucleotides (bp 1-290) to SEQ ID NO: 112, therefore it would hybridize to SEQ ID NO: 112 under stringent hybridization conditions.

The rejection is maintained.

Regarding the art rejections, Applicants argue that since part (d) was amended to cite at least 80% sequence identity over the entire length of SEQ ID NO: 112-115, the art rejections are moot. However, the way claim 1 is constructed, if the limitation of part 1(c) is met, then the whole claim is rejected.

H) Regarding the rejection of claim 15 under 35 U.S.C. 102 (b) as being anticipated by GibcoBRL catalog, Applicants argue that the kit claimed comprises a means for determining the presence of a nucleic acid molecule comprising:"(a) a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 221; (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 112-115; (d) a nucleic acid molecule that hybridizes under stringent hybridization conditions of 50% formamide/6x SSC at 42 C for at least 10 hours or 6X SSC at 68 C without formamide for at least 10 hours to the nucleic acid molecule of (a) or (b); or (d) a nucleic acid molecule having at least 80% sequence identity over the entire length of the nucleic acid molecule of (a) or (b)."

Applicants claim "means for determining a nucleic acid molecule". The Gibco BRL catalog teaches means for detecting any nucleic acid molecule, since they teach a kit comprising random primers, therefore this reference anticipates claim 15.

The rejection is maintained.

Claim Objections

5. Claims 23-27 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 23-27 are drawn to the nucleic acid of claim 1 having at least 85%, at least 90%, at least 95% or at least 98% or at least 89%, respectively, sequence identity to a nucleic acid of claim 1 (a) or (b). However, claim 1 (a) is drawn to a nucleic acid sequence encoding SEQ ID NO: 221 and claim 1(b) is drawn to the nucleic acid comprising SEQ ID NO: 112-115, therefore, claims 23-27 are broader in scope than either claim 1(a) or claim 1(b).

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-5, 7, 8, 15 and 18-27 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a an isolated nucleic acid molecule comprising SEQ ID NO: 112-115, a nucleic acid that hybridizes under stringent hybridization conditions of 50% formamide/6x SSC at 42 C for at least 10 hours or 6X SSC at 68 C without formamide for at least 10 hours to the nucleic acid molecule comprising SEQ ID NO: 112-115 or a nucleic acid having at least 80% sequence identity to SEQ ID NO: 112-115. Claims 18-22 are drawn to a nucleic acid comprising SEQ ID NO: 112, 113, 114, 115 or a nucleic acid encoding SEQ ID NO: 221,

respectively. Claims 23-27 are drawn to the nucleic acid of claim 1 having at least 85%, at least 90%, at least 95%, at least 98% or at least 89% sequence identity to a nucleic acid of claim 1 (a) or (b).

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the nucleic acids. The only cited utilities identified by the examiner are as probes and primers (pages 41-45), protein expression (pages 45-54), production of transgenic animals and cells (pages 89-93), diagnosis of ovarian cancer (pages 95-103), detection of non-cancerous ovarian disease (page 103-104), identifying ovary tissue (page 104-105). These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the nucleic acid comprising SEQ ID NO: 84. No well established utilities for this specific nucleic acid are identified in either the specification.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, as provided by the specification, nucleic acid with SEQ ID NO: 115 has been identified by data mining of sequences in the Incyte Genomics LIFESEQ® database using CLASP software (page 117), and SEQ ID NO: 115 was identified as a CLASP1 sequence, which means that it has detectable tissue-specific expression. The level of expression is shown on page 124 as .0064. No further explanations were provided in the specification regarding SEQ ID NO: 115. It is not clear what was the source of the nucleic acid (cell culture or tumor) and what was the level of expression of SEQ ID NO: 115 in cancer vs. normal cells, therefore it is not

clear how a nucleic acid molecule comprising SEQ ID NO: 115 could be used for detection of ovarian malignancies, especially since the expression of SEQ ID NO: 115 was classified as being ovary-specific, not tumor specific.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). In the instant case, additional research would be necessary to establish substantial utility of a nucleic acid comprising SEQ ID NO: 115.

In order for a polynucleotide to be useful for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in ovarian tissue cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any

information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, then the substantial utility of the nucleic acid comprising SEQ ID NO: 115 is, at best, a relationship to an association with ovary tissue. This utility is not specific because there are a lot of different nucleic acids expressed in ovary tissue, 137 of them provided by Applicants. Thus, the presence of the nucleic acids in ovary tissue does not provide a specific utility because there is no direct or even indirect connection made between any particular utility and the nucleic acid comprising SEQ ID NO: 115. Therefore, even though Applicants claim that the nucleic acids could be used in detection and monitoring of ovarian cancer, no specific association between the ovarian cancer and SEQ ID NO: 115 has been provided, and thus, no specific utility for SEQ ID NO: 115.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5, 7, 8, 15 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The current claims are drawn to a an isolated nucleic acid molecule comprising SEQ ID NO: 112-115, a nucleic acid that hybridizes under stringent hybridization conditions of 50% formamide/6x SSC at 42 C for at least 10 hours or 6X SSC at 68 C without formamide for at least 10 hours to the nucleic acid molecule comprising SEQ ID NO: 112-115 or a nucleic acid having at least 80% sequence identity to SEQ ID NO: 112-115. Claims 18-22 are drawn to a nucleic acid comprising SEQ ID NO: 112, 113, 114, 115 or a nucleic acid encoding SEQ ID NO: 221, respectively. Claims 23-27 are drawn to the nucleic acid of claim 1 having at least 85%, at least 90%, at least 95%, at least 98% or at least 89% sequence identity to a nucleic acid of claim 1 (a) or (b). Applicants assert that nucleic acids with SEQ ID NO: 1-137 can be used for diagnosis of ovarian cancer(pages 95-103), detection of non-cancerous ovarian disease (page 103-104) and identifying ovary tissue (page 104-105). However, as will be further discussed, there is no support in the specification and prior art for the asserted use of the nucleic acid with SEQ ID NO: 115 or its fragments. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Working Examples

The specification has no working examples of using a nucleic acid with SEQ ID NO: 115 for detection of ovarian cancer, non-cancerous ovary disease or in identifying ovary tissue.

Guidance in the Specification.

The specification provides no evidence that the disclosed nucleic acid sequences can be in fact used for detection of ovarian cancer, non-cancerous ovary disease or in identifying ovary tissue. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses that nucleic acid with SEQ ID NO: 115 has been identified by data mining of sequences in the Incyte Genomics LIFESEQ® database using CLASP software (page 117), and SEQ ID NO: 115 was identified as a CLASP1 sequence, which means that it has detectable expression only in ovary tissue. The level of expression is shown on page 124 as .0064. No further explanations were provided in the specification regarding SEQ ID NO: 115. It is not clear what was the source of the nucleic acid (cell culture or tumor) and what was the level of expression of SEQ ID NO: 115 in cancer vs. normal cells, therefore it is not clear how a nucleic acid molecule comprising SEQ ID NO: 115 could be used for detection of ovarian malignancies, for example.

The unpredictability of the art and the state of the prior art

Applicants did not show what type of cells nucleic acid with SEQ ID NO: 115 was obtained from, i.e., whether these cells were from tissue culture or primary tumors. At the time the invention was made, it was known in the prior art that observations of genetic status in cancer cell lines are frequently not observable in primary tumor tissues. For example, Sidransky *et al.* (US 5856094) teach that although the rate of a homozygous deletion of P16 ranged from 40-60% of breast cancer cell lines, neither homozygous deletions nor point mutations are typically observed in primary breast carcinomas (Col. 2, lines 9-14). The suitability of cell lines in general as models for primary

tumors is also questioned in the prior art. For example, Dermer (Bio/Technology, Vol. 12, March 1994, p. 320) teaches that "[w]hen a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary-type step that enables the new cell line to thrive in its artificial environment...Yet normal or malignant cells in vivo are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of the lab dish and in the body has been in the scientific literature for more than 30 years, evidence that has been systematically ignored by the cancer establishment (first column)."

Therefore, if the cells considered were cell culture cells, then it is even more problematic if SEQ ID NO: 115 could be used for detection of ovarian tumors from patients' tissues.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to enable using of nucleic acids with SEQ ID NO: 115 for the detection of ovarian malignancies or ovarian tissue. A person of skill in the art would have to perform detection studies of SEQ ID NO: 115 in normal and malignant ovarian tissues from cell culture and patients' samples, as well as in cells from unrelated tissues, to determine whether there is a difference in the expression levels of SEQ ID NO: 115 in all of these types of cells, and association of SEQ ID NO: 115 with ovarian malignancies. Significance of the increased expression levels needs to be established, as there are usually variations in tissues obtained from different individuals, therefore studies involving statistically significant numbers of patients would also need to be performed.

Conclusion

Given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example it is the position of the examiner that it would require undue experimentation for one of skill in the art to use the claimed nucleic acids for ovarian malignancies detection.

10. Claims 1-5, 7, 8 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to a an isolated nucleic acid molecule comprising SEQ ID NO: 112-115, a nucleic acid that hybridizes under stringent hybridization conditions of 50% formamide/6x SSC at 42 C for at least 10 hours or 6X SSC at 68 C without formamide for at least 10 hours to the nucleic acid molecule comprising SEQ ID NO: 112-115 or a nucleic acid having at least 80% sequence identity to SEQ ID NO: 112-115. Claims 23-27 are drawn to the nucleic acid of claim 1 having at least 85%, at least 90%, at least 95%, at least 98% or at least 89% sequence identity to a nucleic acid of claim 1 (a) or (b).

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species

disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID No: 115 and its subsequences with SEQ ID NO: 112-114. Thus, applicant has express possession of only one particular nucleic acid, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. No written description of alleles, of upstream or downstream regions containing additional sequence has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acid hybridizing under stringent conditions to SEQ ID NO: 115 lack any specific structure, is precisely the situation of naming a

type of material which is generally known to likely exist, but, except for four specific SEQ ID NOs, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "a nucleic acid that shybridizes to the nucleic acid comprising SEQ ID NO: 115 under stringent conditions", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID NO: 112-115. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by a sequence with accession No. BF116062 (October 24, 2000).

Regarding claim 1, sequence with accession No. BF116062 (582 bp) is 20.7% identical to SEQ ID NO: 115, with bp 1 to 582 99.8% identical (one mismatch) to bp 1139-1721 of SEQ ID NO: 115 (see sequence alignment). Therefore, sequence with accession No. BF116062 will hybridize to SEQ ID NO: 115 under stringent conditions.

Regarding claim 2, the nucleic acid with accession No. BF116062 is a cDNA.

Regarding claims 4 and 5, the nucleic acid with accession No. BF116062 is Homo sapiens cDNA.

Regarding claims 7 and 8, the nucleic acid was cloned into pT7T3D vector and DH10B host cells.

13. Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by a sequence with accession No. BE857462 (September 29, 2000).

Regarding claim 1, sequence with accession No. BE857462 (524 bp) is 69.2% identical to SEQ ID NO: 113, with bp 1-524 99.8% identical (one mismatch) to bp 1-524 of SEQ ID NO: 113 (see sequence alignment). Therefore, sequence with accession No. BE857462 will hybridize to SEQ ID NO: 113 under stringent hybridization conditions. In addition, sequence with accession No. BE857462 (582 bp) is 42.5% identical to SEQ ID NO: 112, with bp 359 to 524 99.4% identical (one mismatch) to bp 1-166 of SEQ ID NO: 112 (see sequence alignment). Therefore, sequence

with accession No. BE857462 will hybridize to SEQ ID NO: 112 under stringent hybridization conditions as well.

Regarding claim 2, the nucleic acid with accession No. BE857462 is a cDNA.

Regarding claims 4 and 5, the nucleic acid with accession No. BE857462 is Homo sapiens cDNA.

Regarding claims 7 and 8, the nucleic acid was cloned into pT7T3D vector and DH10B host cells.

14. Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by a sequence with accession No. AA156960 (May 14, 1997) as evidenced by Hillier et al. (Genome Res., vol. 6, pp. 807-828, 1996).

Regarding claim 1, sequence with accession No. AA156960 (495 bp) is 17.2% identical to SEQ ID NO: 115, with bp 1 to 495 99.6% identical (two mismatches) to bp 2240-2736 of SEQ ID NO: 115 (see sequence alignment). Therefore, sequence with accession No. AA156960 will hybridize to SEQ ID NO: 115 under stringent hybridization conditions. In addition, sequence with accession No. AA156960 (495 bp) is 51.5% identical to SEQ ID NO: 114, with bp 1 to 495 99.6% identical (two mismatches) to bp 422-918 of SEQ ID NO: 114 (see sequence alignment). Therefore, sequence with accession No. AA156960 will hybridize to SEQ ID NO: 114 under stringent hybridization conditions as well.

Regarding claim 2, the nucleic acid with accession No. AA156960 is a cDNA.

Regarding claims 4 and 5, the nucleic acid with accession No. AA156960 is human cDNA.

Regarding claims 7 and 8, Hillier et al. evidence that the cDNA clones were in pT7T3Pac vector and host cells (page 821, last paragraph; page 822, second paragraph).

15. Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by a sequence with accession No. AA088637 (May 11, 1997) as evidenced by Hillier et al. (Genome Res., vol. 6, pp. 807-828, 1996).

Regarding claim 1, sequence with accession No. AA088637 (442 bp) is 42.8% identical to SEQ ID NO: 113, with bp 3 to 441 91.6% identical to bp 107-543 of SEQ ID NO: 113 and with 171 contiguous nucleotides (bp 141-311) 100% identical to SEQ ID NO: 113, therefore sequence with accession No. AA088637 will hybridize to SEQ ID NO: 113 under stringent hybridization conditions (see sequence alignment). In addition, sequence with accession No. AA088637 (442 bp) is 31.3% identical to SEQ ID NO: 112, with bp 255-441 87.8% identical to bp 1-185 of SEQ ID NO: 112 and with 56 contiguous nucleotides (bp 1-56) 100% identical to SEQ ID NO: 112 (see sequence alignment). Therefore, sequence with accession No. AA088637 will hybridize to SEQ ID NO: 112 under stringent hybridization conditions as well.

Regarding claim 2, the nucleic acid with accession No. AA088637 is a cDNA.

Regarding claims 4 and 5, the nucleic acid with accession No. AA088637 is human cDNA.

Regarding claims 7 and 8, Hillier et al. evidence that the cDNA clones were in pT7T3Pac vector and host cells (page 821, last paragraph; page 822, second paragraph).

16. Claims 1, 2, 4, 5, 7, 8, 15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Rosen et al. (US 2003/0108907).

Regarding claim 1, Rosen et al. teach polynucleotides and polypeptides related to ovarian and breast cancers (Abstract). Rosen et al. teach a polynucleotide with SEQ ID NO: 947 (1593 bp) (sequence listing), which is 77% identical to SEQ ID NO: 12, 70.5% identical to SEQ ID NO: 13, 94.4% identical to SEQ ID NO: 14 and 55% identical to SEQ ID NO: 115 (see sequence alignments). The sequence with SEQ ID NO: 947 is 100% identical over 613 nucleotides (bp 1393-2005) and 586

nucleotides (bp 2153-2738) to SEQ ID NO: 115, therefore it would hybridize to SEQ ID NO: 115 under stringent hybridization conditions. The sequence with SEQ ID NO: 947 is 100% identical over 576 nucleotides (bp 343-918) to SEQ ID NO: 114, therefore it would hybridize to SEQ ID NO: 114 under stringent hybridization conditions. The sequence with SEQ ID NO: 947 is also 100% identical over 407 nucleotides (bp 242-648) to SEQ ID NO: 113, therefore it would hybridize to SEQ ID NO: 113 under stringent hybridization conditions. Finally, the sequence with SEQ ID NO: 947 is 100% identical over 291 nucleotides (bp 1-290) to SEQ ID NO: 112, therefore it would hybridize to SEQ ID NO: 112 under stringent hybridization conditions.

Regarding claim 2, Rosen et al. teach polynucleotides being cDNAs (page 2, [0018]).

Regarding claims 4 and 5, Rosen et al. teach human polynucleotides (page 2, [0015]).

Regarding claims 7 and 8, Rosen et al. teach vectors and host cell comprising the polynucleotides (page 1, [0003]; page 98, [[0177]-[0179]).

Regarding claim 15, Rosen et al. teach a kit for analyzing samples for the presence of cancerous polynucleotides, the kit comprising at least one polynucleotide probe (page 120, [0363];

Regarding claim 17, Rosen et al. teach polynucleotides administered as vaccines (page 117, [0325]); page 132, [0460]).

17. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by GibcoBRL Catalog (p. 7-7, 1993-94).

GibcoBRL catalog teaches a kit with random primers (hexamers), which are suitable for DNA synhesis (page 7.7). Therefore, since any DNA can be amplified with such primers, they can be used to detect the nucleic acid comprising SEQ ID NO: 115.

18. No references were found teaching or suggesting claim 3, but it is rejected for reasons given above.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
8/10/09

JEFFREY FREDMAN
PRIMARY EXAMINER
8/11/09